cyanoalkyl, etc; R4 = alkyl, cycloalkyl(alkyl), aryl(alkyl); R5 = H; R6 = OH; R5R6 = :O; R7R8 = (un)substituted (CH2)3, (CH2)4, with 1 CH2 optionally replaced by NH, N(acyl), S, etc., optionally carrying 1 fused cycloalkane or (hetero)aromatic ring; R9 = alkoxycarbonyl, monoalkylcarbamoyl, CONHCHR10CONHR11; R10, R11 = alkyl; n = 0, 1] and their pharmaceutically acceptable salts were prepared, e.g., by coupling amines H2NCHR4CR5R6CH2NR7CHR8R9 with acids R1R2NCHR3CO2H. Thus, N1-isobutyl-L-isoleucylamide (preparation given) was coupled with Z-proline succinimide ester (Z = benzyloxycarbonyl), the resulting dipeptide was deprotected and coupled with (Z-phenylalanyl)methyl bromide, the intermediate tripeptide reduced by NaBH4 in EtOH, deprotected, and coupled with Z-Asn-OH to give N2-[N-[3(S)-[(Z-asparaginyl)amino]-2(R,S)-hydroxy-4-phenylbutyl]-L-prolyl]-N1-isobutyl-L-isoleucylamide. One (unspecified) of 2 isomers of the latter in vitro inhibited human immunodeficiency virus protease with an IC50 of 0.13 μM. IC50 values reported for 7 other I ranged from 0.01-0.87 μM.

=>

---Logging off of STN---

Connection closed by remote host
END

Unable to generate the STN prompt.
Exiting the script...

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:ssptamxg1614

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

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NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	SEP 09	ACD predicted properties enhanced in REGISTRY/ZREGISTRY
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NEWS 5	OCT 04	CA/CAplus-Canadian Intellectual Property Office (CIPO) added to core patent offices
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CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
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FILE 'HOME' ENTERED AT 16:11:10 ON 30 NOV 2005

=> file caplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

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FILE LAST UPDATED: 29 Nov 2005  (20051129/ED)

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=> s us5599984/pn
L1            3 US5599984/PN

=> sel rn
E1 THROUGH E112 ASSIGNED

=> file registry
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
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FULL ESTIMATED COST                                     2.58       2.79

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TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

  Please note that search-term pricing does apply when
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**********************************************************************
*                                                                    *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,   *
* effective March 20, 2005.  A new display format, IDERL, is now    *
* available and contains the CA role and document type information. *
*                                                                    *
**********************************************************************
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Structure search iteration limits have been increased. See HELP SLIMITS
for details.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

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               4/BI OR 169764-92-5/BI OR 169764-93-6/BI OR 169764-94-7/BI OR
               169764-95-8/BI OR 169764-98-1/BI OR 169764-99-2/BI OR 169765-02-
               0/BI OR 169765-03-1/BI OR 169765-04-2/BI OR 169765-05-3/BI OR
               169765-06-4/BI OR 169765-07-5/BI OR 169765-09-7/BI OR 169765-11-
               1/BI OR 169765-12-2/BI OR 169765-13-3/BI OR 169765-14-4/BI OR
               169765-16-6/BI OR 169765-17-7/BI OR 169765-22-4/BI OR 169765-23-
               5/BI OR 169765-24-6/BI OR 169765-25-7/BI OR 169765-26-8/BI OR
               169765-27-9/BI OR 169765-28-0/BI OR 169765-29-1/BI OR 169765-30-
               4/BI OR 169765-32-6/BI OR 169765-34-8/BI OR 169765-35-9/BI OR
               169765-36-0/BI OR 169765-37-1/BI OR 1937-1

=> s l3 and (p38 or MPK2 or RK or ERK1 or ERK2 or HOG1)
           349 P38
             9 MPK2
           593 RK
```

```
            90 ERK1
            53 ERK2
            15 HOG1
L4           0 L3 AND (P38 OR MPK2 OR RK OR ERK1 OR ERK2 OR HOG1)

=> s l3 and (mitogen (S) activated)
          1875 MITOGEN
          5092 ACTIVATED
          1798 MITOGEN (S) ACTIVATED
L5           0 L3 AND (MITOGEN (S) ACTIVATED)

=> s l3 and (extracellular (S) signal)
          2763 EXTRACELLULAR
         16601 SIGNAL
           204 EXTRACELLULAR (S) SIGNAL
L6           0 L3 AND (EXTRACELLULAR (S) SIGNAL)

=> file caplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    47.72      50.51

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=> s l2
L7       248429 L2

=> s l7 and (p38 or MPK2 or RK or ERK1 or ERK2 or HOG1)
          11180 P38
             22 MPK2
           1959 RK
           9281 ERK1
           8825 ERK2
            235 HOG1
L8           673 L7 AND (P38 OR MPK2 OR RK OR ERK1 OR ERK2 OR HOG1)

=> s l8 and HIV
          63538 HIV
L9           10 L8 AND HIV

=> d 1-10 bib abs

L9   ANSWER 1 OF 10  CAPLUS  COPYRIGHT 2005 ACS on STN
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AN 2005:259881 CAPLUS
DN 142:336517
TI Preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivatives for their use as modulators of the androgen receptor in a tissue selective manner
IN Kaufman, Mildred L.; Meissner, Robert S.; Mitchell, Helen J.
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 127 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005025572	A1	20050324	WO 2004-US28655	20040902

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2003-501789P P 20030910
OS MARPAT 142:336517
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB 17-Heterocyclic-4-aza-5α-androst-1-en-3-one derivs., such as I [dashed bond = single bond, double bond; X = H, halo; Y, Z = H, alkyl, halo; Y and Z, together with the carbon atom to which they are attached = cyclopropyl; n = 0-3; U, V, W, D = CH, N, S, O; R1 = H, CF3, carbonyl(alkyl), OH, alkoxy, halo, alkyl, CH2OH, alkylamino; R2 = halo, carbonyl(alkyl), carbonyl(alkenyl), carbonyl(alkynyl), alkenylamino, heterocyclic, etc.], were prepared for their use as modulators of the androgen receptor (AR) in a tissue selective manner. Thus, II (R = OH) was treated with Et3N, and iso-Bu chloroformate, followed by reaction with N,O-dimethylhydroxylamine hydrochloride to give II [R = N(Me)OMe (III)]. III was converted to 4-aza-5α-androst-1-en-3,20-dione derivative II (R = Me), and then to bromide II [R = CH2Br (IV)], which was treated with N-butyl-thiourea to afford V. The prepared compds. are useful in the enhancement of weakened muscle tone and the treatment of conditions caused by androgen deficiency or which can be ameliorated by androgen administration, including osteoporosis, osteopenia, glucocorticoid-induced osteoporosis, periodontal disease, bone fracture, bone damage following bone reconstructive surgery, sarcopenia, frailty, aging skin, male hypogonadism, postmenopausal symptoms in women, atherosclerosis, hypercholesterolemia, hyperlipidemia, obesity, aplastic anemia and other hematopoietic disorders, inflammatory arthritis and joint repair, **HIV**-wasting, prostate cancer, benign prostatic hyperplasia (BPH), abdominal adiposity, metabolic syndrome, type II diabetes, cancer cachexia, Alzheimer's disease, muscular dystrophies, cognitive decline, sexual dysfunction, sleep apnea, depression, premature ovarian failure, and autoimmune disease, alone or in combination with other active agents.
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2004:823936 CAPLUS
DN 141:325786
TI Long-acting conjugates of biologically active compounds with macromolecules, and their therapeutic use
IN Silva, Abelardo; Erickson, John E.; Eissenstat, Michael; Afonina, Elena; Gulnik, Sergei
PA Sequoia Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 173 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004085505	A2	20041007	WO 2004-US8847	20040324

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2003-456472P	P	20030324	
US 2003-456952P	P	20030325	
US 2003-518892P	P	20031110	

OS MARPAT 141:325786
AB The invention provides biol. active compds. that may be reacted with macromols., e.g. albumin, to form covalently linked complexes, wherein the resulting complexes exhibit a desired biol. activity in vivo. More specifically, the complexes are isolated complexes comprising a biol. active moiety covalently bound to a linking group and a protein. The complexes are prepared by conjugating a biol. active moiety, e.g. a renin inhibitor or a viral fusion inhibitor peptide, with purified and isolated protein. The complexes have extended lifetimes in the bloodstream as compared to the unconjugated mol., and exhibit biol. activity for extended periods of time as compared to the unconjugated mol. The invention also provides antiviral compds. that are inhibitors of viral infection and/or exhibit anti-fusiogenic properties. In particular, the invention provides compds. having inhibiting activity against viruses such as human immunodeficiency virus (**HIV**), respiratory syncytial virus (RSV), human parainfluenza virus (HPV), measles virus (MeV), and simian immunodeficiency virus (SIV) and that have extended duration of action for the treatment of viral infections.

L9 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:292020 CAPLUS
DN 140:321233
TI A preparation of pyrrole derivatives useful for the treatment of disorders ameliorated by reduction of TNF-α production and/or **p38** activity
IN Bullington, James L.; Fan, Xiaodong; Jackson, Paul F.; Zhang, Yue-mei
PA Janssen Pharmaceutica N.V., Belg.
SO PCT Int. Appl., 116 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004029040	A1	20040408	WO 2003-US30223	20030924

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

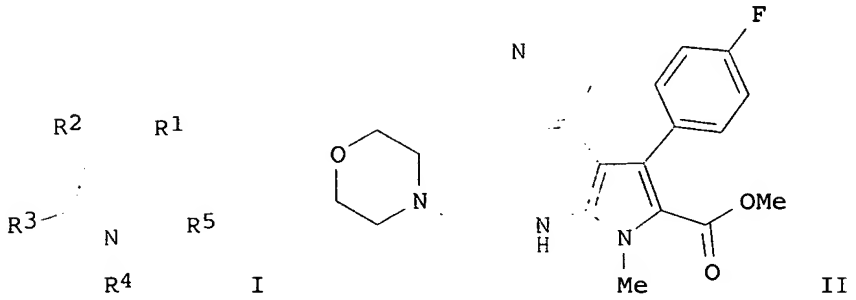
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

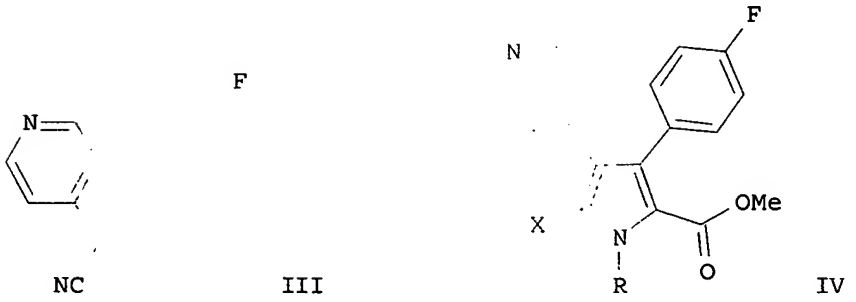
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2500221	AA	20040408	CA 2003-2500221		20030924
US 2005043331	A1	20050224	US 2003-670031		20030924
EP 1549635	A1	20050706	EP 2003-770442		20030924
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
BR 2003014783	A	20050726	BR 2003-14783		20030924
PRAI US 2002-414436P	P	20020927			
WO 2003-US30223	W	20030924			

OS MARPAT 140:321233

GI





AB The invention relates to 3-pyridyl-4-arylpyrrole derivs. of formula I [wherein: R1 and R2 are independently selected from (un)substituted (hetero)aryl; R3 = H, (un)substituted alkyl, -N:CR6-, -C(O)R7, etc.; R4 = H, (un)substituted alkyl, (un)substituted (hetero)aryl, etc.; R5 = (un)substituted alkyl, C(O)OR7, C(O)R7, CN, NO2, halo, etc.; R6 and R7 are independently selected from H, (un)substituted alkyl, (un)substituted aryl, (un)substituted heterocycle; with provisos], and pharmaceutical compns. comprising the same, useful for treating disorders ameliorated by reducing TNF-α production and/or **p38** activity in appropriate cells. The invention compds. I were screened for p38 inhibition (in-vitro enzyme assays) and TNF-α inhibition (in-vitro whole cell assays and in vivo rodent assay). The invention also provides therapeutic and prophylactic methods using the instant pharmaceutical compns. For instance, pyrrole derivative II (compound 5; mouse 10 mg/kg, 0.5 h, 44% inhibition of TNF-α production) was prepared via condensation of 4-fluorobenzaldehyde with 4-pyridylacetonitrile, heterocyclization of the

obtained pyridine derivative III with Me isocyanoacetate, N-methylation of the pyrrole ring of the obtained pyrrolecarboxylate derivative IV (X = H, R = H), bromination of the pyrrolecarboxylate derivative IV (X = H, R = Me), and subsequent amination of the obtained bromopyrrole derivative IV (X = Br, R = Me) by 4-(2-aminoethyl)morpholine.

L9 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:888761 CAPLUS
DN 137:380050
TI Peptide inhibitors of receptor activator of NF-κB (RANK), and therapeutic use
IN Aggarwal, Bharat; Darnay, Bryant G.; Singh, Sujay
PA Research Development Foundation, USA
SO PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002092623	A1	20021121	WO 2002-US14842	20020510
	WO 2002092623	C1	20040108		
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2447431	AA	20021121	CA 2002-2447431	20020510
	EP 1385872	A1	20040204	EP 2002-725988	20020510
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2005503349	T2	20050203	JP 2002-589506	20020510
PRAI	US 2001-290429P	P	20010511		
	WO 2002-US14842	W	20020510		

AB The invention provides a RANK (receptor activator of NF-κB) inhibitor consisting of a TRAF-6 (TNF receptor-associated factor-6) binding domain attached to a leader sequence. The peptide inhibitor inhibits RANKL (RANK ligand)-mediated osteoclast differentiation, thus indicating that targeted disruption of interaction between RANK and TRAF6 may prove useful as a therapeutic for metabolic bone disorders, leukemia, arthritis, and metastatic cancer of the bone.
RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:783142 CAPLUS
DN 137:293428
TI Human Immunodeficiency Virus Type 1 (**HIV**-1) Tat Induces Nitric-oxide Synthase in Human Astroglia
AU Liu, Xiaojuan; Jana, Malabendu; Dasgupta, Subhajit; Koka, Sreenivas; He, Jun; Wood, Charles; Pahan, Kalipada
CS Department of Oral Biology, University of Nebraska Medical Center, Lincoln, NE, 68583, USA
SO Journal of Biological Chemistry (2002), 277(42), 39312-39319
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
AB Human immunodeficiency virus type 1 (**HIV**-1) infection is known to cause neuronal injury and dementia in a significant proportion of patients. However, the mechanism by which **HIV**-1 mediates its

deleterious effects in the brain is poorly defined. The present study was undertaken to investigate the effect of the **HIV**-1 tat gene on the expression of inducible nitric-oxide synthase (iNOS) in human U373MG astroglial cells and primary astroglia. Expression of the tat gene as RSV-tat but not that of the CAT gene as RSV-CAT in U373MG astroglial cells led to the induction of NO production and the expression of iNOS protein and mRNA. Induction of NO production by recombinant **HIV**-1 Tat protein and inhibition of RSV-tat-induced NO production by anti-Tat antibodies suggest that RSV-tat-induced production of NO is dependent on Tat and that Tat is secreted from RSV-tat-transfected astroglia. Similar to U373MG astroglial cells, RSV-tat also induced the production of NO in human primary astroglia. The induction of human iNOS promoter-derived luciferase activity by the expression of RSV-tat suggests that RSV-tat induces the transcription of iNOS. To understand the mechanism of induction of iNOS, we investigated the role of NF-κB and C/EBPβ, transcription factors responsible for the induction of iNOS. Activation of NF-κB as well as C/EBPβ by RSV-tat, stimulation of RSV-tat-induced production of NO by the wild type of p65 and C/EBPβ, and inhibition of RSV-tat-induced production of NO by Δp65, a dominant-neg. mutant of p65, and ΔC/EBPβ, a dominant-neg. mutant of C/EBPβ, suggest that RSV-tat induces iNOS through the activation of NF-κB and C/EBPβ. In addition, we show that extracellular signal-regulated kinase (ERK) but not that **p38** mitogen-activated protein kinase (MAPK) is involved in RSV-tat induced production of NO. Interestingly, PD98059, an inhibitor of the ERK pathway, and .DELTA.**ERK2**, a dominant-neg. mutant of **ERK2**, inhibited RSV-tat-induced production of NO through the inhibition of C/EBPβ but not that of NF-κB. This study illustrates a novel role for **HIV**-1 tat in inducing the expression of iNOS in human astrocytes that may participate in the pathogenesis of **HIV**-associated dementia.

RE.CNT 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:31330 CAPLUS
DN 134:95509
TI Method of reducing neuronal injury or apoptosis using a **p38** mitogen-activated protein kinase inhibitor
IN Lipton, Stuart A.
PA USA
SO PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001001986	A1	20010111	WO 2000-US18385	20000630
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2373883	AA	20010111	CA 2000-2373883	20000630
	EP 1196167	A1	20020417	EP 2000-948576	20000630
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2003503456	T2	20030128	JP 2001-507478	20000630
	AU 777275	B2	20041007	AU 2000-62052	20000630
	US 2003078274	A1	20030424	US 2002-115578	20020402
PRAI	US 1999-142341P	P	19990702		

US 2000-608572 B1 20000630
WO 2000-US18385 W 20000630
OS MARPAT 134:95509
AB A method is provided for reducing neuronal injury or apoptosis including administering to a patient in need thereof an effective amount of a **p38** mitogen-activated protein kinase (MAPK) inhibitor. Methods of treating an **HIV**-mediated dementia, glaucoma, or other neurodegenerative disorders are also disclosed.
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2000:910634 CAPLUS
DN 134:176557
TI **HIV** gp120 enhances NO production by cardiac myocytes through **p38** MAP kinase-mediated NF-κB activation
AU Kan, Hong; Xie, Zirong; Finkel, Mitchell S.
CS Department of Medicine Robert C. Byrd Health Sciences Center, West Virginia University School of Medicine, Morgantown, WV, 26506-9157, USA
SO American Journal of Physiology (2000), 279(6, Pt. 2), H3138-H3143
CODEN: AJPHAP; ISSN: 0002-9513
PB American Physiological Society
DT Journal
LA English
AB Human immunodeficiency virus (**HIV**) infection is associated with a surprisingly high frequency of myocardial dysfunction. Potential mechanisms include direct effects of **HIV**, indirect effects mediated by cytokines, or a combination. We have previously reported that interleukin-1β (IL-1β) (500 U/mL) alone induced nitric oxide (NO) production by neonatal rat cardiac myocytes (CM). Effects of the **HIV**-1 envelope, glycoprotein120 (gp120), on inducible NO synthase (iNOS) in CM have not been previously reported. Unlike IL-1β, recombinant **HIV**-gp120 (1 μg/mL) alone failed to enhance NO production in CM (0.5±0.4 vs. 0.4±0.5 μmol/1.25+105 cells/48 h, gp120 vs. control, resp.). However, the addition of gp120 to IL-1β significantly enhanced iNOS mRNA expression (70±1.5 vs. 26±2.4 optical units, IL-1β + gp120 vs. IL-1β, resp.), iNOS protein synthesis (42±1.4 vs. 18±0.8 optical units, IL-1β + gp120 vs. IL-1β, resp.), and NO production (NO2-) (6.6±0.6 vs. 4.1±0.8 μmol/1.25+105 cells/48 h, IL-1β + gp120 vs. IL-1β, resp.). **HIV**-gp120 enhancement of IL-1β-induced NO2- production was blocked by 10 μM of SB-203580 (SB), a selective **p38** protein kinase inhibitor (3.6±0.2 vs. 6.6±0.6 μmol/1.25+105 cells/48 h, IL-1β + gp120 + SB vs. IL-1β + gp120, resp.). **HIV**-gp120-enhanced **p38** protein kinase activity was associated with an increase in IL-1β-stimulated NF-κB activity (184±12.7 vs. 92±10.7 optical units, IL-1β + gp120 vs. IL-1β, resp.). None of these effects was seen with another recombinant **HIV**-1 protein, Tat. Thus **HIV**-gp120 enhancement of IL-1β-induced NO production is associated with **p38** -mediated activation of NF-κB. Direct effects of **HIV** -gp120 on CM may provide a previously unrecognized mechanism contributing to **HIV** cardiomyopathy.
RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2000:771367 CAPLUS
DN 134:41038
TI Phosphorothioate backbone modification modulates macrophage activation by CpG DNA
AU Sester, David P.; Naik, Shalin; Beasley, Shannon J.; Hume, David A.; Stacey, Katryn J.
CS Institute for Molecular Bioscience and Departments of Microbiology and Biochemistry, University of Queensland, Brisbane, 4072, Australia

SO Journal of Immunology (2000), 165(8), 4165-4173
CODEN: JOIMA3; ISSN: 0022-1767
PB American Association of Immunologists
DT Journal
LA English
AB Macrophages respond to unmethylated CpG motifs present in nonmammalian DNA. Stabilized phosphorothioate-modified oligodeoxynucleotides (PS-ODN) containing CpG motifs form the basis of immunotherapeutic agents. In this study, we show that PS-ODN do not perfectly mimic native DNA in activation of macrophages. CpG-containing PS-ODN were active at 10- to 100-fold lower concns. than corresponding phosphodiester ODN in maintenance of cell viability in the absence of CSF-1, in induction of NO production, and in activation of the IL-12 promoter. These enhancing effects are attributable to both increased stability and rate of uptake of the PS-ODN. By contrast, PS-ODN were almost inactive in down-modulation of the CSF-1R from primary macrophages and activation of the **HIV**-1 LTR. Delayed or poor activation of signaling components may contribute to this, as PS-ODN were slower and less effective at inducing phosphorylation of the extracellular signal-related kinases 1 and 2. In addition, at high concns., non-CpG PS-ODN specifically inhibited responses to CpG DNA, whereas nonstimulatory phosphodiester ODN had no such effect. Although nonstimulatory PS-ODN caused some inhibition of ODN uptake, this did not adequately explain the levels of inhibition of activity. The results demonstrate that the phosphorothioate backbone has both enhancing and inhibitory effects on macrophage responses to CpG DNA.
RE.CNT 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2000:221229 CAPLUS
DN 133:29514
TI Thermal hyperalgesia and mechanical allodynia produced by intrathecal administration of the human immunodeficiency virus-1 (**HIV**-1) envelope glycoprotein, gp120
AU Milligan, E. D.; Mehmert, K. K.; Hinde, J. L.; Harvey, L. O.; Martin, D.; Tracey, K. J.; Maier, S. F.; Watkins, L. R.
CS Department of Psychology, University of Colorado at Boulder, Boulder, CO, USA
SO Brain Research (2000), 861(1), 105-116
CODEN: BRREAP; ISSN: 0006-8993
PB Elsevier Science B.V.
DT Journal
LA English
AB Astrocytes and microglia in the spinal cord have recently been reported to contribute to the development of peripheral inflammation-induced exaggerated pain states. Both lowering of thermal pain threshold (thermal hyperalgesia) and lowering of response threshold to light tactile stimuli (mech. allodynia) have been reported. The notion that spinal cord glia are potential mediators of such effects is based on the disruption of these exaggerated pain states by drugs thought to preferentially affect glial function. Activation of astrocytes and microglia can release many of the same substances that are known to mediate thermal hyperalgesia and mech. allodynia. The aim of the present series of studies was to determine whether exaggerated pain states could also be created in rats by direct, intraspinal immune activation of astrocytes and microglia. The immune stimulus used was peri-spinal (intrathecal, i.t.) application of the Human Immunodeficiency Virus type 1 (**HIV**-1) envelope glycoprotein, gp120. This portion of **HIV**-1 is known to bind to and activate microglia and astrocytes. Robust thermal hyperalgesia (tail-flick, TF, and Hargreaves tests) and mech. allodynia (von Frey and touch-evoked agitation tests) were observed in response to i.t. gp120. Heat denaturing of the complex protein structure of gp120 blocked gp120-induced thermal hyperalgesia. Lastly, both thermal hyperalgesia and mech. allodynia to i.t. gp120 were blocked by spinal pretreatment with drugs (fluorocitrate and CNI-1493) thought to preferentially disrupt glial function.

RE.CNT 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:338118 CAPLUS
DN 129:36435
TI Guanylhydrazones useful for treating diseases associated with T-cell activation
IN Tracey, Kevin; Cohen, Pamela; Bukrinsky, Michael; Schmidtmayerova, Helena
PA Picower Institute for Medical Research, USA
SO PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9820868	A1	19980522	WO 1997-US20670	19971114
	W: AL, AU, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IL, IS, JP, KR, KZ, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SI, SK, TR, UA, UZ, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2271693	AA	19980522	CA 1997-2271693	19971114
	AU 9854360	A1	19980603	AU 1998-54360	19971114
	AU 746647	B2	20020502		
	EP 963197	A1	19991215	EP 1997-948263	19971114
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	US 6143728	A	20001107	US 1997-970973	19971114
	JP 2001503775	T2	20010321	JP 1998-522801	19971114
	US 6673777	B1	20040106	US 2000-705581	20001102
	US 2004171695	A1	20040902	US 2003-619426	20030716
PRAI	US 1996-31061P	P	19961115		
	US 1997-970973	A3	19971114		
	WO 1997-US20670	W	19971114		
	US 2000-705581	A1	20001102		

OS MARPAT 129:36435
AB There is disclosed a method for treating diseases and disorders involving T-cell activation and **HIV**-infection, using the **p38** mitogen-activated protein kinase (MAPK) signaling pathway as a target for intervention. There is further disclosed a use for guanylhydrazone-substituted compds. to treat diseases and disorders related to T cell activation and **HIV**-infection.
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
=> s l7 (L) (p38 or MPK2 or RK or ERK1 or ERK2 or HOG1)
         11180 P38
            22 MPK2
          1959 RK
          9281 ERK1
          8825 ERK2
           235 HOG1
L10        190 L7 (L) (P38 OR MPK2 OR RK OR ERK1 OR ERK2 OR HOG1)

=> s l10 and inhibit?
       1789419 INHIBIT?
L11        174 L10 AND INHIBIT?

=> d 170-174 bib abs
```

L11 ANSWER 170 OF 174 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:408507 CAPLUS

DN 129:144658
TI SB 203580 **inhibits** p38 mitogen-activated protein kinase, nitric oxide production, and inducible nitric oxide synthase in bovine cartilage-derived chondrocytes
AU Badger, Alison M.; Cook, Michael N.; Lark, Michael W.; Newman-Tarr, Tonie M.; Swift, Barbara A.; Nelson, Allen H.; Barone, Frank C.; Kumar, Sanjay
CS Departments of Bone and Cartilage Biology and Cardiovascular Pharmacology, SmithKline Beecham Pharmaceuticals, King of Prussia, PA, 19406, USA
SO Journal of Immunology (1998), 161(1), 467-473
CODEN: JOIMA3; ISSN: 0022-1767
PB American Association of Immunologists
DT Journal
LA English
AB Nitric oxide (NO) is implicated in a number of inflammatory processes and is an important mediator in animal models of rheumatoid arthritis and in in vitro models of cartilage degradation The pyridinyl imidazole SB 203580 **inhibits** p38 mitogen-activated protein (MAP) kinase in vitro, blocks proinflammatory cytokine production in vitro and in vivo, and is effective in animal models of arthritis. The purpose of this study was to determine whether SB 203580 could **inhibit** p38 MAP kinase activity, NO production, and inducible NO synthase (iNOS) in IL-1 stimulated bovine articular cartilage/chondrocyte cultures. The results indicated that SB 203580 **inhibited** both IL-1 stimulated p38 MAP kinase activity in isolated chondrocytes and NO production in bovine chondrocytes and cartilage explants with an IC50 value of approx. 1 μM. To **inhibit** NO production, SB 203580 had to be present in cartilage explant cultures during the first 8 h of IL-1 stimulation, and activity was lost when it was added 24 h following IL-1. SB 203580 did not **inhibit** iNOS activity, as measured by the conversion of arginine to citrulline, when added directly to cultures where the enzyme had already been induced, but had to be present during the induction period. Using a 372-bp probe for bovine iNOS we demonstrated **inhibition** of IL-1-induced mRNA by SB 203580 at both 4 and 24 h following IL-1 treatment. The iNOS mRNA levels were consistent with NO levels in 24-h cell culture supernatants of the IL-1-stimulated bovine chondrocytes used to obtain the RNA.
RE.CNT 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 171 OF 174 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:403996 CAPLUS
DN 129:135005
TI Interleukin-1β-induced rat pancreatic islet nitric oxide synthesis requires both the p38 and extracellular signal-regulated kinase 1/2 mitogen-activated protein kinases
AU Larsen, Claus M.; Wadt, Karin A. W.; Juhl, Lone F.; Andersen, Henrik U.; Karlsen, Allan E.; Su, Michael S.-S.; Seedorf, Klaus; Shapiro, Leland; Dinarello, Charles A.; Mandrup-Poulsen, Thomas
CS Univ. Colorado Health Sciences Center, Denver, CO, 80262, USA
SO Journal of Biological Chemistry (1998), 273(24), 15294-15300
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
AB Interleukin-1β (IL-1β) is cytotoxic to rat pancreatic β-cells by **inhibiting** glucose oxidation, causing DNA damage, and inducing apoptosis. Nitric oxide (NO) is a necessary but not sufficient mediator of these effects. IL-1β induced kinase activity toward Elk-1, activation transcription factor 2, c-Jun, and heat shock protein 25 in rat islets. By Western blotting with phosphospecific antibodies and by immunocomplex kinase assay, IL-1β was shown to activate extracellular signal-regulated kinase (ERK) 1/2 and p38 mitogen-activated protein kinase (p38) in islets and rat insulinoma cells. Specific ERK1/2 and p38 **inhibitors** individually reduced but in combination blocked IL-1β-mediated islet NO synthesis, and reverse transcription-polymerase chain reaction of inducible NO synthase mRNA

showed that ERK1/2 and p38 controlled IL-1β-induced islet inducible NO synthase expression at the transcriptional level. Hyperosmolarity caused phosphorylation of Elk-1, activation of transcription factor 2, and heat shock protein 25, and activation of ERK1/2 and p38 in islets comparable to that induced by IL-1β but did not lead to NO synthesis. **Inhibition** of p38 but not of ERK1/2 attenuated IL-1β-mediated **inhibition** of glucose-stimulated insulin release. Thus, ERK1/2 and p38 activation is necessary but not sufficient for IL-1β-mediated β-cell NO synthesis and p38 is involved in signaling of NO-independent effects of IL-1β in β-cells.

RE.CNT 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 172 OF 174 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:129074 CAPLUS
DN 128:256329
TI Extracellular signal-regulated kinase and p38 subgroups of mitogen-activated protein kinases regulate inducible nitric oxide synthase and tumor necrosis factor-α gene expression in endotoxin-stimulated primary glial cultures
AU Bhat, Narayan R.; Zhang, Peisheng; Lee, John C.; Hogan, Edward L.
CS Department of Neurology, Medical University of South Carolina, Charleston, SC, 29425, USA
SO Journal of Neuroscience (1998), 18(5), 1633-1641
CODEN: JNRSDS; ISSN: 0270-6474
PB Society for Neuroscience
DT Journal
LA English
AB Tumor necrosis factor-α (TNFα) and nitric oxide (NO), the product of inducible NO synthase (iNOS), mediate inflammatory and immune responses in the CNS under a variety of neuropathol. situations. They are produced mainly by "activated" astrocytes and microglia, the two immune regulatory cells of the CNS. Here, the authors examined the regulation of TNFα and iNOS gene expression in endotoxin-stimulated primary glial cultures, focusing on the role of mitogen-activated protein (MAP) kinase cascades. The bacterial lipopolysaccharide (LPS) was able to activate extracellular signal-regulated kinase (ERK) and p38 kinase subgroups of MAP kinases in microglia and astrocytes. ERK activation was sensitive to PD98059, the kinase **inhibitor** that is specific for ERK kinase. The activity of p38 kinase was **inhibited** by SB203580, a member of the novel class of cytokine suppressive anti-inflammatory drugs (CSAIDs), as revealed by blocked activation of the down-stream kinase, MAP kinase-activated protein kinase-2. The treatment of glial cells with either LPS alone (microglia) or a combination of LPS and interferon-γ (astrocytes) resulted in an induced production of NO and TNFα. The two kinase **inhibitors**, at micromolar concns., individually suppressed and, in combination, almost completely blocked glial production of NO and the expression of iNOS and TNFα, as determined by Western blot anal. Reverse transcriptase-PCR anal. showed changes in iNOS mRNA levels that paralleled iNOS protein and NO while indicating a lack of effect of either of the kinase **inhibitors** on TNFα mRNA expression. The results demonstrate key roles for ERK and p38 MAP kinase cascades in the transcriptional and post-transcriptional regulation of iNOS and TNFα gene expression in endotoxin-activated glial cells.

RE.CNT 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 173 OF 174 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1997:734919 CAPLUS
DN 128:59787
TI Blockade of p38 mitogen-activated protein kinase pathway **inhibits** inducible nitric-oxide synthase expression in mouse astrocytes
AU Da Silva, Jean; Pierrat, Benoit; Mary, Jean-Luc; Lesslauer, Werner
CS Dep. Cent. Nervous System diseases, PRPN, F. Hoffmann-La Roche, Ltd., Basel, 4070, Switz.

SO Journal of Biological Chemistry (1997), 272(45), 28373-28380
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
AB Treatment of mouse astrocyte cultures with combined interleukin (IL)-1α and tumor necrosis factor (TNF)-α induced expression of inducible nitric-oxide synthase (iNOS), resulting in sustained release of large amts. of nitric oxide, whereas TNF-α and IL-1α individually were unable to induce iNOS expression in astrocytes. The role of MAPK cascades and of NF-κB activation in the early intracellular signal transduction involved in iNOS transcription in TNF-α/IL-1α-stimulated astrocytes was investigated. TNF-α and IL-1α activated all p42/44MAPK, p38MAPK, AND P54JNK pathways as determined by immunopptn. kinase assays using specific antibodies and substrates. The p38MAPK pathway is specifically involved in TNF-α/IL-1α-induced iNOS expression, since iNOS protein and nitric oxide release in the presence of a specific **inhibitor** of p38MAPK, 4-(4-fluorophenyl)-2-2-(4-hydroxyphenyl)-5-(4-pyridyl)-imidazole (FHPI), were dramatically diminished. In contrast, PD98059, a specific **inhibitor** of MEK1 had no effect on iNOS expression. P38MAPK did not couple NF-κB to iNOS transcription, but NF-κB had a clear role in iNOS transcription regulation. Northern blot anal. showed that the p38MAPK pathway controlled iNOS expression at the transcriptional level, since iNOS mRNA was reduced in the presence of FHPI in TNF-α/IL-1α-stimulated astrocytes. INOS expression was investigated with TNF receptor (TNFR)-1- and TNFR-2-deficient mice. The TNF-α activity in TNF-α-stimulated astrocytes was exclusively mediated through TNFR-1, most likely because TNFR-2-mediated signals in astrocytes dd not connect to the p38MAPK pathway. These data suggest that TNF-α/IL-1α-induced iNOS expression depends on a yet undetd. second pathway in addition to p38MAPK.
RE.CNT 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 174 OF 174 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1997:211817 CAPLUS
DN 126:276157
TI p38 mitogen-activated protein kinase down-regulates nitric oxide and up-regulates prostaglandin E2 biosynthesis stimulated by interleukin-1β
AU Guan, Zhonghong; Baier, Lisa D.; Morrison, Aubrey R.
CS Department Molecular Biology Pharmacology Medicine, Washington University School Medicine, St. Louis, MO, 63110, USA
SO Journal of Biological Chemistry (1997), 272(12), 8083-8089
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
AB The inflammatory cytokine interleukin 1β (IL-1β) induces both cyclooxygenase-2 (Cox-2) and the inducible nitric-oxide synthase (iNOS) with increases in the release of prostaglandins (PGs) and nitric oxide (NO) from glomerular mesangial cells. However, the intracellular signaling mechanisms by which IL-1β induces iNOS and Cox2 expression is obscure. Our current studies demonstrate that IL-1β produces a rapid increase in p38 mitogen-activated protein kinase (MAPK) phosphorylation and activation. Serum starvation and SC68376, a drug which selectively **inhibits** p38 MAPK in mesangial cells, were used to investigate whether p38 MAPK contributes to the signaling mechanism of IL-1β induction of NO and PG synthesis. Serum starvation and SC68376 selectively **inhibited** IL-1β-induced activation of p38 MAPK. Both SC68376 and serum starvation enhanced NO biosynthesis by increasing iNOS mRNA expression, protein expression, and nitrite production In contrast, both SC68376 and serum starvation suppressed PG release by **inhibiting** Cox2 mRNA, protein expression, and PGE2

synthesis. These data demonstrate that IL-1β phosphorylates and activates p38 MAPK in mesangial cells. The activation of p38 MAPK may provide a crucial signaling mechanism, which mediates the up-regulation of PG synthesis and the down-regulation of NO biosynthesis induced by IL-1β.

```
=> s l10
         11180 P38
            22 MPK2
          1959 RK
          9281 ERK1
          8825 ERK2
           235 HOG1
L12         190 L7 (L) (P38 OR MPK2 OR RK OR ERK1 OR ERK2 OR HOG1)

=> d 185-190 bib abs
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L12 ANSWER 185 OF 190 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:408507 CAPLUS
DN 129:144658
TI SB 203580 inhibits p38 mitogen-activated protein kinase, nitric oxide production, and inducible nitric oxide synthase in bovine cartilage-derived chondrocytes
AU Badger, Alison M.; Cook, Michael N.; Lark, Michael W.; Newman-Tarr, Tonie M.; Swift, Barbara A.; Nelson, Allen H.; Barone, Frank C.; Kumar, Sanjay
CS Departments of Bone and Cartilage Biology and Cardiovascular Pharmacology, SmithKline Beecham Pharmaceuticals, King of Prussia, PA, 19406, USA
SO Journal of Immunology (1998), 161(1), 467-473
CODEN: JOIMA3; ISSN: 0022-1767
PB American Association of Immunologists
DT Journal
LA English
AB Nitric oxide (NO) is implicated in a number of inflammatory processes and is an important mediator in animal models of rheumatoid arthritis and in in vitro models of cartilage degradation The pyridinyl imidazole SB 203580 inhibits p38 mitogen-activated protein (MAP) kinase in vitro, blocks proinflammatory cytokine production in vitro and in vivo, and is effective in animal models of arthritis. The purpose of this study was to determine whether SB 203580 could inhibit p38 MAP kinase activity, NO production, and inducible NO synthase (iNOS) in IL-1 stimulated bovine articular cartilage/chondrocyte cultures. The results indicated that SB 203580 inhibited both IL-1 stimulated p38 MAP kinase activity in isolated chondrocytes and NO production in bovine chondrocytes and cartilage explants with an IC50 value of approx. 1 μM. To inhibit NO production, SB 203580 had to be present in cartilage explant cultures during the first 8 h of IL-1 stimulation, and activity was lost when it was added 24 h following IL-1. SB 203580 did not inhibit iNOS activity, as measured by the conversion of arginine to citrulline, when added directly to cultures where the enzyme had already been induced, but had to be present during the induction period. Using a 372-bp probe for bovine iNOS we demonstrated inhibition of IL-1-induced mRNA by SB 203580 at both 4 and 24 h following IL-1 treatment. The iNOS mRNA levels were consistent with NO levels in 24-h cell culture supernatants of the IL-1-stimulated bovine chondrocytes used to obtain the RNA.
RE.CNT 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD
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L12 ANSWER 186 OF 190 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:403996 CAPLUS
DN 129:135005
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AU Larsen, Claus M.; Wadt, Karin A. W.; Juhl, Lone F.; Andersen, Henrik U.;

Karlsen, Allan E.; Su, Michael S.-S.; Seedorf, Klaus; Shapiro, Leland; Dinarello, Charles A.; Mandrup-Poulsen, Thomas

CS Univ. Colorado Health Sciences Center, Denver, CO, 80262, USA

SO Journal of Biological Chemistry (1998), 273(24), 15294-15300
CODEN: JBCHA3; ISSN: 0021-9258

PB American Society for Biochemistry and Molecular Biology

DT Journal

LA English

AB Interleukin-1β (IL-1β) is cytotoxic to rat pancreatic β-cells by inhibiting glucose oxidation, causing DNA damage, and inducing apoptosis. Nitric oxide (NO) is a necessary but not sufficient mediator of these effects. IL-1β induced kinase activity toward Elk-1, activation transcription factor 2, c-Jun, and heat shock protein 25 in rat islets. By Western blotting with phosphospecific antibodies and by immunocomplex kinase assay, IL-1β was shown to activate extracellular signal-regulated kinase (ERK) 1/2 and p38 mitogen-activated protein kinase (p38) in islets and rat insulinoma cells. Specific ERK1/2 and p38 inhibitors individually reduced but in combination blocked IL-1β-mediated islet NO synthesis, and reverse transcription-polymerase chain reaction of inducible NO synthase mRNA showed that ERK1/2 and p38 controlled IL-1β-induced islet inducible NO synthase expression at the transcriptional level. Hyperosmolarity caused phosphorylation of Elk-1, activation of transcription factor 2, and heat shock protein 25, and activation of ERK1/2 and p38 in islets comparable to that induced by IL-1β but did not lead to NO synthesis. Inhibition of p38 but not of ERK1/2 attenuated IL-1β-mediated inhibition of glucose-stimulated insulin release. Thus, ERK1/2 and p38 activation is necessary but not sufficient for IL-1β-mediated β-cell NO synthesis and p38 is involved in signaling of NO-independent effects of IL-1β in β-cells.

RE.CNT 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 187 OF 190 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1998:129074 CAPLUS

DN 128:256329

TI Extracellular signal-regulated kinase and p38 subgroups of mitogen-activated protein kinases regulate inducible nitric oxide synthase and tumor necrosis factor-α gene expression in endotoxin-stimulated primary glial cultures

AU Bhat, Narayan R.; Zhang, Peisheng; Lee, John C.; Hogan, Edward L.

CS Department of Neurology, Medical University of South Carolina, Charleston, SC, 29425, USA

SO Journal of Neuroscience (1998), 18(5), 1633-1641
CODEN: JNRSDS; ISSN: 0270-6474

PB Society for Neuroscience

DT Journal

LA English

AB Tumor necrosis factor-α (TNFα) and nitric oxide (NO), the product of inducible NO synthase (iNOS), mediate inflammatory and immune responses in the CNS under a variety of neuropathol. situations. They are produced mainly by "activated" astrocytes and microglia, the two immune regulatory cells of the CNS. Here, the authors examined the regulation of TNFα and iNOS gene expression in endotoxin-stimulated primary glial cultures, focusing on the role of mitogen-activated protein (MAP) kinase cascades. The bacterial lipopolysaccharide (LPS) was able to activate extracellular signal-regulated kinase (ERK) and p38 kinase subgroups of MAP kinases in microglia and astrocytes. ERK activation was sensitive to PD98059, the kinase inhibitor that is specific for ERK kinase. The activity of p38 kinase was inhibited by SB203580, a member of the novel class of cytokine suppressive anti-inflammatory drugs (CSAIDs), as revealed by blocked activation of the down-stream kinase, MAP kinase-activated protein kinase-2. The treatment of glial cells with either LPS alone (microglia) or a combination of LPS and interferon-γ (astrocytes) resulted in an induced production of NO and

TNFα. The two kinase inhibitors, at micromolar concns., individually suppressed and, in combination, almost completely blocked glial production of NO and the expression of iNOS and TNFα, as determined by Western blot anal. Reverse transcriptase-PCR anal. showed changes in iNOS mRNA levels that paralleled iNOS protein and NO while indicating a lack of effect of either of the kinase inhibitors on TNFα mRNA expression. The results demonstrate key roles for ERK and p38 MAP kinase cascades in the transcriptional and post-transcriptional regulation of iNOS and TNFα gene expression in endotoxin-activated glial cells.

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DN 128:59787
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AU Da Silva, Jean; Pierrat, Benoit; Mary, Jean-Luc; Lesslauer, Werner
CS Dep. Cent. Nervous System diseases, PRPN, F. Hoffmann-La Roche, Ltd., Basel, 4070, Switz.
SO Journal of Biological Chemistry (1997), 272(45), 28373-28380
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
AB Treatment of mouse astrocyte cultures with combined interleukin (IL)-1α and tumor necrosis factor (TNF)-α induced expression of inducible nitric-oxide synthase (iNOS), resulting in sustained release of large amts. of nitric oxide, whereas TNF-α and IL-1α individually were unable to induce iNOS expression in astrocytes. The role of MAPK cascades and of NF-κB activation in the early intracellular signal transduction involved in iNOS transcription in TNF-α/IL-1α-stimulated astrocytes was investigated. TNF-α and IL-1α activated all p42/44MAPK, p38MAPK, AND P54JNK pathways as determined by immunopptn. kinase assays using specific antibodies and substrates. The p38MAPK pathway is specifically involved in TNF-α/IL-1α-induced iNOS expression, since iNOS protein and nitric oxide release in the presence of a specific inhibitor of p38MAPK, 4-(4-fluorophenyl)-2-2-(4-hydroxyphenyl)-5-(4-pyridyl)-imidazole (FHPI), were dramatically diminished. In contrast, PD98059, a specific inhibitor of MEK1 had no effect on iNOS expression. P38MAPK did not couple NF-κB to iNOS transcription, but NF-κB had a clear role in iNOS transcription regulation. Northern blot anal. showed that the p38MAPK pathway controlled iNOS expression at the transcriptional level, since iNOS mRNA was reduced in the presence of FHPI in TNF-α/IL-1α-stimulated astrocytes. INOS expression was investigated with TNF receptor (TNFR)-1- and TNFR-2-deficient mice. The TNF-α activity in TNF-α-stimulated astrocytes was exclusively mediated through TNFR-1, most likely because TNFR-2-mediated signals in astrocytes dd not connect to the p38MAPK pathway. These data suggest that TNF-α/IL-1α-induced iNOS expression depends on a yet undetd. second pathway in addition to p38MAPK.

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AN 1997:211817 CAPLUS
DN 126:276157
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AU Guan, Zhonghong; Baier, Lisa D.; Morrison, Aubrey R.
CS Department Molecular Biology Pharmacology Medicine, Washington University School Medicine, St. Louis, MO, 63110, USA
SO Journal of Biological Chemistry (1997), 272(12), 8083-8089

CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
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L12 ANSWER 190 OF 190 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1984:434133 CAPLUS
DN 101:34133
TI RK bacterial test for independently measuring chemical toxicity and mutagenicity: short-term forward selection assay
AU Hayes, Sidney; Gordon, Alasdair; Sadowski, Ivan; Hayes, Connie
CS Coll. Med., Univ. Saskatchewan, Saskatoon, SK, S7N 0W0, Can.
SO Mutation Research (1984), 130(2), 97-106
CODEN: MUREAV; ISSN: 0027-5107
DT Journal
LA English
AB A short-term bacterial assay system for determining the mutagenic potential of environmental substances was developed and validated. Genotoxic activity was demonstrated for selected substances from 10 categories of chemical agents. The RK test results were obtained with 1 Escherichia coli assay strain that was transiently exposed to, and then removed from the test substance prior to the selection step for mutant cells. The RK test employs a hitherto unused short-term assay technique for selecting forward mutations in the wild-type selector strain cells. The cells of the selector strain are killed upon shifting to 42° as a consequence of thermal derepression and subsequent expression of the replication genes from an integrated 10-kilobase fragment of phage λ. Cells that acquire mutations in the responsible killing genes are detected by their colony-forming ability of 42°. A substance is determined to be genotoxic if it is capable of increasing the forward mutation frequency for appearance of these mutant cells. Toxicity of the agent is independently evaluated by examining its effect on the viability of the selector strain at 30°, when the viral replication genes remain repressed. The flexible assay protocol enables determination of the effect of pH on mutagenic activity, the requirement for metabolic activation, and assays of nearly insol. or highly toxic substances.

=>

---Logging off of STN---

```
=>
Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    95.70     146.21

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                   -15.33     -15.33

STN INTERNATIONAL LOGOFF AT 16:17:28 ON 30 NOV 2005


Connecting via Winsock to STN



Welcome to STN International!  Enter x:x

LOGINID:ssptamxg1614

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2


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 NEWS  4  OCT 03   MATHDI removed from STN
 NEWS  5  OCT 04   CA/CAplus-Canadian Intellectual Property Office (CIPO) added
                   to core patent offices
 NEWS  6  OCT 13   New CAS Information Use Policies Effective October 17, 2005
 NEWS  7  OCT 17   STN(R) AnaVist(TM), Version 1.01, allows the export/download
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 NEWS 10  OCT 27   EPFULL enhanced with additional content
 NEWS 11  NOV 14   CA/CAplus - Expanded coverage of German academic research

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               CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 13 JUNE 2005.
               V8.0 USERS CAN OBTAIN THE UPGRADE TO V8.01 AT
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FILE 'HOME' ENTERED AT 16:20:03 ON 30 NOV 2005

=> index health
COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.21       0.21

INDEX 'ABI-INFORM, ADISCTI, ADISINSIGHT, ADISNEWS, AQUALINE, AQUASCI,
       BIOBUSINESS, BIOCOMMERCE, BIOENG, BIOSIS, BIOTECHNO, CANCERLIT, CAPLUS,
       CBNB, CEN, CHEMLIST, CIN, CONFSCI, CSNB, DISSABS, EMBAL, EMBASE, ENERGY,
       ENVIROENG, ESBIOBASE, FEDRIP, FOMAD, ...' ENTERED AT 16:20:22 ON 30 NOV 2005

54 FILES IN THE FILE LIST IN STNINDEX

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=> s (guanylhydrazone or amidinohydrazone)
          24   FILE ADISCTI
           6   FILE ADISINSIGHT
           1   FILE ADISNEWS
           1   FILE AQUALINE
           7   FILE AQUASCI
          26   FILE BIOBUSINESS
          17   FILE BIOENG
         825   FILE BIOSIS
         206   FILE BIOTECHNO
         540   FILE CANCERLIT
        1458   FILE CAPLUS
           1   FILE CBNB
           7   FILE CHEMLIST
           1   FILE CIN
          53   FILE CONFSCI
          40   FILE DISSABS
         665   FILE EMBASE
          24   FILE ENERGY
         123   FILE ESBIOBASE
           1   FILE FEDRIP
           4   FILE FROSTI
           4   FILE HEALSAFE
           1   FILE HSDB
          77   FILE IFIPAT
          18   FILE INIS
          28   FILE IPA
          33   FILE JICST-EPLUS
           1   FILE KOSMET
         144   FILE LIFESCI
         644   FILE MEDLINE
          11   FILE NIOSHTIC
           3   FILE NLDB
           7   FILE NTIS
         368   FILE PASCAL
           3   FILE POLLUAB
          12   FILE PROMT
          48   FILE RTECS
         635   FILE SCISEARCH
         862   FILE TOXCENTER
         323   FILE USPATFULL
          19   FILE USPAT2
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          1    FILE WATER

  42 FILES HAVE ONE OR MORE ANSWERS,    54 FILES SEARCHED IN STNINDEX

L1    QUE (GUANYLHYDRAZONE OR AMIDINOHYDRAZONE)

=> d rank
F1          1458   CAPLUS
F2           862   TOXCENTER
F3           825   BIOSIS
F4           665   EMBASE
F5           644   MEDLINE
F6           635   SCISEARCH
F7           540   CANCERLIT
F8           368   PASCAL
F9           323   USPATFULL
F10          206   BIOTECHNO
F11          144   LIFESCI
F12          123   ESBIOBASE
F13           77   IFIPAT
F14           53   CONFSCI
F15           48   RTECS
F16           40   DISSABS
F17           33   JICST-EPLUS
F18           28   IPA
F19           26   BIOBUSINESS
F20           24   ADISCTI
F21           24   ENERGY
F22           19   USPAT2
F23           18   INIS
F24           17   BIOENG
F25           12   PROMT
F26           11   NIOSHTIC
F27            7   AQUASCI
F28            7   CHEMLIST
F29            7   NTIS
F30            6   ADISINSIGHT
F31            4   FROSTI
F32            4   HEALSAFE
F33            3   NLDB
F34            3   POLLUAB
F35            1   ADISNEWS
F36            1   AQUALINE
F37            1   CBNB
F38            1   CIN
F39            1   FEDRIP
F40            1   HSDB
F41            1   KOSMET
F42            1   WATER


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                                                         ENTRY    SESSION
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```
=> s (guanylhydrazone or amidinohydrazone)
          1141 GUANYLHYDRAZONE
           408 AMIDINOHYDRAZONE
L2        1458 (GUANYLHYDRAZONE OR AMIDINOHYDRAZONE)

=> s l2 (L) (MAP or MPK2 or HOG1 or RK or p38 or ERK1 ro ERK2 or JNK or "c-jun" or
CSBP)
         87625 MAP
            22 MPK2
           235 HOG1
          1959 RK
         11180 P38
          9281 ERK1
         30433 RO
          8825 ERK2
             0 ERK1 RO ERK2
                 (ERK1(W)RO(W)ERK2)
          7340 JNK
       3384316 "C"
         14368 "JUN"
         11865 "C-JUN"
                 ("C"(W)"JUN")
           110 CSBP
L3          11 L2 (L) (MAP OR MPK2 OR HOG1 OR RK OR P38 OR ERK1 RO ERK2 OR JNK
               OR "C-JUN" OR CSBP)

=> d 5-11 bib abs

L3   ANSWER 5 OF 11  CAPLUS  COPYRIGHT 2005 ACS on STN
AN   1999:191926  CAPLUS
DN   130:351008
TI   Role of interleukin (IL)-2 receptor β-chain subdomains and Shc in p38
     mitogen-activated protein (MAP) kinase and p54 MAP kinase
     (stress-activated protein kinase/c-Jun N-terminal kinase) activation.
     IL-2-driven proliferation is independent of p38 and p54 MAP kinase
     activation
AU   Hunt, Abigail E.; Lali, Ferdinand V.; Lord, James D.; Nelson, Brad H.;
     Miyazaki, Tadaaki; Tracey, Kevin J.; Foxwell, Brian M. J.
CS   Kennedy Institute of Rheumatology, Hammersmith, London, W6 8LH, UK
SO   Journal of Biological Chemistry (1999), 274(11), 7591-7597
     CODEN: JBCHA3; ISSN: 0021-9258
PB   American Society for Biochemistry and Molecular Biology
DT   Journal
LA   English
AB   The authors have shown recently that interleukin (IL)-2 activates the
     mitogen-activated protein (MAP) kinase family members
     p38 (HOG1/stress-activated protein kinase II) and p54 (
     c-Jun N-terminal kinase/stress-activated protein kinase
     I). Furthermore, the p38 MAP kinase inhibitor
     SB203580 inhibited IL-2-driven T cell proliferation, suggesting that
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p38 MAP kinase might be involved in mediating proliferative signals. Here, using transfected BA/F3 cell lines, it is shown that both the acidic domain and the membrane-proximal serine-rich region of the IL-2Rβ chain are required for **p38** and p54 **MAP** kinase activation and that, as for p42/44 **MAP** kinase, this activation requires the Tyr338 residue of the acidic domain, the binding site for Shc. It is well established that the acidic domain of the IL-2Rβ chain is dispensable for IL-2-driven proliferation, and thus the authors' observations suggest that neither **p38** nor p54 **MAP** kinase activation is required for IL-2-driven proliferation of BA/F3 cells. In addition, the tetravalent **guanylhydrazone** inhibitor of proinflammatory cytokine production, CNI-1493, can block the activation of p54 and **p38 MAP** kinases by IL-2 but has no effect on IL-2-driven proliferation of BA/F3 cells, activated primary T cells, or a cytotoxic T cell line. Furthermore, the authors' observations provide evidence for the existence of an addnl., unknown target of the **p38 MAP** kinase inhibitor SB203580, the activation of which is essential for mitogenic signaling by IL-2.

RE.CNT 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:765627 CAPLUS
DN 130:138239
TI Fetuin (α2-HS-glycoprotein) opsonizes cationic macrophage-deactivating molecules
AU Wang, Haichao; Zhang, Minghuang; Bianchi, Marina; Sherry, Barbara; Sama, Andrew; Tracey, Kevin J.
CS Department of Emergency Medicine, The Picower Institute for Medical Research, North Shore University Hospital-New York University School of Medicine, Manhasset, NY, 11030, USA
SO Proceedings of the National Academy of Sciences of the United States of America (1998), 95(24), 14429-14434
CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal
LA English
AB Macrophages become activated by bacterial endotoxin (lipopolysaccharide) and other stimuli to release proinflammatory cytokines and NO. To prevent release of toxic or potentially lethal quantities of these factors, the state of macrophage activation is counter-regulated by anti-inflammatory mediators (e.g., glucocorticoid hormones, interleukin 10, and transforming growth factor type β). Fetuin, a neg. acute-phase protein, recently was implicated as an anti-inflammatory mediator, because it is required for macrophage deactivation by spermine. In the present studies, the authors found that fetuin is necessary for macrophages to respond to CNI-1493, a tetravalent **guanylhydrazone** inhibitor of **p38** mitogen-activated protein kinase phosphorylation. Fetuin dose-dependently increases macrophage uptake of CNI-1493, which can be specifically inhibited by anti-human fetuin antibodies. Anti-human fetuin antibodies render primary human peripheral blood mononuclear cells insensitive to deactivation by CNI-1493. Thus, macrophages use fetuin as an opsonin for cationic-deactivating mols., both endogenous (e.g., spermine) and pharmacol. (e.g., CNI-1493). This role of fetuin as an opsonic participant in macrophage-deactivating mechanisms has implications for understanding and manipulating the innate immune response.

RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:338118 CAPLUS
DN 129:36435
TI Guanylhydrazones useful for treating diseases associated with T-cell activation
IN Tracey, Kevin; Cohen, Pamela; Bukrinsky, Michael; Schmidtmayerova, Helena

PA Picower Institute for Medical Research, USA
SO PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9820868	A1	19980522	WO 1997-US20670	19971114
	W: AL, AU, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IL, IS, JP, KR, KZ, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SI, SK, TR, UA, UZ, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2271693	AA	19980522	CA 1997-2271693	19971114
	AU 9854360	A1	19980603	AU 1998-54360	19971114
	AU 746647	B2	20020502		
	EP 963197	A1	19991215	EP 1997-948263	19971114
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	US 6143728	A	20001107	US 1997-970973	19971114
	JP 2001503775	T2	20010321	JP 1998-522801	19971114
	US 6673777	B1	20040106	US 2000-705581	20001102
	US 2004171695	A1	20040902	US 2003-619426	20030716
PRAI	US 1996-31061P	P	19961115		
	US 1997-970973	A3	19971114		
	WO 1997-US20670	W	19971114		
	US 2000-705581	A1	20001102		

OS MARPAT 129:36435
AB There is disclosed a method for treating diseases and disorders involving T-cell activation and HIV-infection, using the **p38** mitogen-activated protein kinase (MAPK) signaling pathway as a target for intervention. There is further disclosed a use for **guanylhydrazone**-substituted compds. to treat diseases and disorders related to T cell activation and HIV-infection.
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1997:408565 CAPLUS
DN 127:107891
TI The critical role of p38 MAP kinase in T cell HIV-1 replication
AU Cohen, Pamela S.; Schmidtmayerova, Helena; Dennis, Jameel; Dubrovsky, Larisa; Sherry, Barbara; Wang, Haichao; Bukrinsky, Michael; Tracey, Kevin J.
CS The Picower Institute for Medical Research, Manhasset, NY, 11030, USA
SO Molecular Medicine (New York) (1997), 3(5), 339-346
CODEN: MOMEF3; ISSN: 1076-1551
PB Springer
DT Journal
LA English
AB Replication of HIV-1 in human T lymphocytes requires the activation of host cellular proteins. This study identifies **p38** mitogen-activated protein kinase (MAPK) as one such kinase necessary for HIV-1 replication in T cells. Primary human T lymphocytes were infected with the LAI strain of HIV-1 and Jurkat cells were infected with the RF strain of HIV-1. HIV replication was measured by reverse transcriptase activity. Cellular expression of endogenous **p38** MAPK protein was analyzed using immunopptn. Blockade of **p38** MAPK expression was achieved using antisense oligonucleotides to **p38** MAPK and the **guanylhydrazone** compound CNI-1493, an inhibitor of **p38** MAPK activation. HIV-1 infection of both primary human T lymphocytes and a T cell line rapidly activated the cellular **p38** MAPK pathway, which remained activated for the duration of the culture. Addition of phosphothioated antisense oligonucleotides to **p38** MAPK

specifically inhibited viral replication. Blockade of **p38** MAPK activation by addition of CNI-1493 also inhibited HIV-1 viral replication of primary T lymphocytes in a dose- and time-dependent manner. Stimulation of **p38** MAPK activation did not occur with the addition of heat-inactivated virus, suggesting that viral internalization, and not just membrane binding, is necessary for **p38** MAPK activation. These results indicate that activation of the **p38** MAPK cascade is critical for HIV-1 replication in primary T lymphocytes, and that blockade of this signal transduction pathway may be a novel therapeutic approach to the treatment of HIV-1 infection.

RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1989:54604 CAPLUS
DN 110:54604
TI The effects of polyamine biosynthesis inhibitors on infection of Hordeum vulgare L. by Erysiphe graminis f.sp. hordei Marchal
AU West, H. M.; Walters, D. R.
CS Dep. Plant Sci., West Scotland Coll., Ayr, KA6 5HW, UK
SO New Phytologist (1988), 110(2), 193-200
CODEN: NEPHAV; ISSN: 0028-646X
DT Journal
LA English
AB The effects of the inhibitors of polyamine biosynthesis, 2-difluoromethylornithine (DFMO), (E)-2-(fluoromethyl)dehydroornithine (Δ-MFMO), (E)-2-(fluoromethyl) dehydroornithine Me ester (Δ-MFMO.CH3), 2-hydrazinoornithine, (2R,5R)-6-heptyne-2,5-diamine (RR-**MAP**), 2-difluoromethylarginine (DFMA), cyclohexylamine (CHA) and methylgloxal-bis(**guanylhydrazone**) (MGBG), on infection of barley leaves (H. vulgare) by E. graminis hordei, were examined Various concns. of the inhibitors were sprayed onto barley leaves cv. Golden Promise as post-inoculation treatments. DFMO, MGBG and a combination of the two were also applied as pre-inoculation treatments. Each inhibitor substantially reduced mildew infection. DFMO was as efficient as the more recently developed ornithine analog. With the exception of the DFMA treatments, post-inoculation sprays were more effective than pre-inoculation ones. When DFMO, MGBG and DFMA were sprayed onto leaves at different times, DFMO and MGBG most effectively controlled mildew when sprayed on the third day after inoculation. DFMA was more efficient as a pre-inoculation treatment. Addition of polyamines to DFMO sprays increased mildew infection, compared to that resulting from the DFMO treatment alone, but infection was less than in the controls.

L3 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1988:432496 CAPLUS
DN 109:32496
TI Polyamines and insulin production in isolated mouse pancreatic islets
AU Welsh, Nils; Sjoeholm, Aake
CS Dep. Med. Cell Biol., Uppsala Univ., Uppsala, S-751 23, Swed.
SO Biochemical Journal (1988), 252(3), 701-7
CODEN: BIJOAK; ISSN: 0306-3275
DT Journal
LA English
AB The role of polyamines in the metabolism and insulin production of pancreatic islet cells was studied in cells from adult mice used either immediately or after tissue culture. There was a significant decrease in the islet content of spermidine during culture, although the effect was less pronounced with a high glucose concentration Furthermore, a stimulatory effect of a high glucose concentration, as compared with low glucose, on the content of spermine was observed To elucidate further the role of polyamines in β-cell physiol., the ornithine decarboxylase inhibitors difluoromethylornithine (DFMO) and methylacetylenic putrescine (**MAP**) and the S-adenosylmethionine decarboxylase inhibitor

ethylglyoxal bis(**guanylhydrazone**) (EGBG) were added to the culture media. Addition of DFMO together with **MAP** decreased the cellular contents of putrescine and spermidine, whereas the content of spermine was unaffected. When EGBG was added in combination with DFMO and **MAP**, there was a decrease in the content of spermine also. Cell viability in the islets depleted of their polyamine contents was not impaired, as assessed by detns. of oxygen uptake rates and ATP contents. Depletion of putrescine plus spermidine by addition of DFMO + **MAP** was associated with decreased biosynthesis of (pro)insulin and total protein. When the content of spermine was decreased also by the further addition of EGBG, the decrease in (pro)insulin biosynthesis was more pronounced and was paralleled by a decrease in the insulin mRNA content. Under these conditions, the glucose-stimulated insulin release, the insulin content, and the rates of islet DNA synthesis were also decreased. Thus, putrescine and spermidine are necessary for the maintenance of normal insulin and protein biosynthesis, whereas spermine may exert a role in some other cellular processes, such as DNA replication, RNA transcription and glucose-stimulated insulin release.

L3 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1971:35579 CAPLUS
DN 74:35579
TI Application of the symbolic addition procedure in neutron diffraction for noncentrosymmetric crystals
AU Sikka, S. K.
CS Nucl. Phys. Div., Bhabha At. Res. Cent., Bombay, India
SO Acta Crystallographica, Section A: Crystal Physics, Diffraction, Theoretical and General Crystallography (1970), 26(6), 662-6
CODEN: ACACBN; ISSN: 0567-7394
DT Journal
LA English
AB For noncentrosymmetric crystals containing both pos. and neg. scatterers of neutrons, the symbolic addition procedure has been tested as a means of obtaining phases of neutron reflections. Test calcns. were done for 2 structures, α-resorcinol and methylglyoxal bis(**guanylhydrazone**)-2HCl.H2O (I), which have already been studied by neutron diffraction using conventional methods. This procedure yields the phase angles with reasonable accuracy. The average error in phases for α-resorcinol was 14°, and the F0 Fourier synthesis with these phases revealed the position of all the pos. scatterers and 3 out of 6 H atoms. The average error in I was 40°, and only 10 pos. scattering atoms out of 16 could be clearly seen in the Fourier **map.** For both structures an F0 **map** was superior to an E **map.** When the contribution of the neg. scatterers to the total neutron scattering is <25%, the symbolic addition method will apply for crystals containing up to 100 atoms per unit cell.

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=> index health
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

INDEX 'ABI-INFORM, ADISCTI, ADISINSIGHT, ADISNEWS, AQUALINE, AQUASCI,
       BIOBUSINESS, BIOCOMMERCE, BIOENG, BIOSIS, BIOTECHNO, CANCERLIT, CAPLUS,
       CBNB, CEN, CHEMLIST, CIN, CONFSCI, CSNB, DISSABS, EMBAL, EMBASE, ENERGY,
       ENVIROENG, ESBIOBASE, FEDRIP, FOMAD, ...' ENTERED AT 16:57:35 ON 30 NOV 2005

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=> s 164301-51-3/rn
          0*  FILE ABI-INFORM
          0*  FILE ADISCTI
          0*  FILE ADISINSIGHT
          0*  FILE ADISNEWS
          0*  FILE AQUALINE
          0*  FILE AQUASCI
          0*  FILE BIOBUSINESS
          0*  FILE BIOCOMMERCE
          0*  FILE BIOENG
          0*  FILE BIOSIS
          0*  FILE BIOTECHNO
          0*  FILE CANCERLIT
         59   FILE CAPLUS
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          0*  FILE ENVIROENG
          0*  FILE ESBIOBASE
          0*  FILE FEDRIP
          0*  FILE FOMAD
          0*  FILE FOREGE
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          0*  FILE IFIPAT
          0*  FILE INIS
          0*  FILE IPA
          0*  FILE JICST-EPLUS
          0*  FILE KOSMET
          0*  FILE LIFESCI
          0*  FILE MEDLINE
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          0*  FILE NAPRALERT
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          0*  FILE PASCAL
          0*  FILE POLLUAB
          0*  FILE PROMT
          0*  FILE SCISEARCH
          0*  FILE TOXCENTER
         31   FILE USPATFULL
          0*  FILE WATER
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2 FILES HAVE ONE OR MORE ANSWERS, 54 FILES SEARCHED IN STNINDEX

L1 QUE 164301-51-3/RN

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accessing the remaining file names entered.
ENTER A FILE NAME OR (IGNORE):
ENTER A FILE NAME OR (IGNORE):end

=> file caplus

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FULL ESTIMATED COST	0.59	0.80

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FILE LAST UPDATED: 29 Nov 2005 (20051129/ED)

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=> s 164301-51-3/rn
59 164301-51-3
0 164301-51-3D
L2 59 164301-51-3/RN
(164301-51-3 (NOTL) 164301-51-3D)

=> d 59 bib abs

L2 ANSWER 59 OF 59 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1995:558462 CAPLUS
DN 123:25357
TI An inhibitor of macrophage arginine transport and nitric oxide production (CNI-1493) prevents acute inflammation and endotoxin lethality
AU Bianchi, Marina; Ulrich, Peter; Bloom, Ona; Meistrell, Malcolm III; Zimmerman, Gary A.; Schmidtmayerova, Helena; Bukrinsky, Michael; Donnelley, Thomas; Bucala, Richard; et al.
CS Picower Institute for Medical Research, Mannhasset, NY, 11030, USA
SO Molecular Medicine (Baltimore, MD, United States) (1995), 1(3), 254-66
CODEN: MOMEF3; ISSN: 1076-1551
DT Journal
LA English
AB Nitric oxide (NO), a small effector mol. produced enzymically from L-arginine by nitric oxide synthase (NOS), is a mediator not only of

important homeostatic mechanisms (e.g., blood vessel tone and tissue perfusion), but also of key aspects of local and systemic inflammatory responses. Previous efforts to develop inhibitors of NOS to protect against NO-mediated tissue damage in endotoxin shock have been unsuccessful, largely because such competitive NOS antagonists interfere with critical vasoregulatory NO production in blood vessels and decrease survival in endotoxemic animals. Accordingly, we sought to develop a pharmaceutical approach to selectively inhibit NO production in macrophages while sparing NO responses in blood vessels. The processes of cytokine-inducible L-arginine transport and NO production were studied in the murine macrophage-like cell line (RAW 264.7). A series of multivalent guanylhydrazones were synthesized to inhibit cytokine-inducible L-arginine transport. One such compound (CNI-1493) was studied further in animal models of endothelial-derived relaxing factor (EDRF) activity, carrageenan inflammation, and lethal lipopolysaccharide (LPS) challenge. Upon activation with cytokines, macrophages increase transport of L-arginine to support the production of NO by NOS. Since endothelial cells do not require this addnl. arginine transport to produce NO, we reasoned that a competitive inhibitor of cytokine-inducible L-arginine transport would not inhibit EDRF activity in blood vessels, and thus might be effectively employed against endotoxic shock. CNI-1493, a tetravalent guanyl-hydrazone, proved to be a selective inhibitor of cytokine-inducible arginine transport and NO production, but did not inhibit EDRF activity. In mice, CNI-1493 prevented the development of carrageenan-induced footpad inflammation, and conferred protection against lethal LPS challenge. A selective inhibitor of cytokine-inducible L-arginine transport that does not inhibit vascular EDRF responses is effective against endotoxin lethality and significantly reduces inflammatory responses.

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            59 164301-51-3
             0 164301-51-3D
L3          59 164301-51-3/RN
                 (164301-51-3 (NOTL) 164301-51-3D )

=> d 55-58
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L3 ANSWER 55 OF 59 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1996:286869 CAPLUS
DN 124:332241
TI CNI-1493 inhibits monocyte/macrophage tumor necrosis factor by suppression of translation efficiency
AU Cohen, Pamela S.; Nakshatri, Harikrishna; Dennis, Jameel; Caragine, Theresa; Bianchi, Marina; Cerami, Anthony; Tracey, Kevin J.
CS Lab. Biomed. Sci., Picower Inst. Med. Res., Manhasset, NY, 11030, USA
SO Proceedings of the National Academy of Sciences of the United States of America (1996), 93(9), 3967-3971
CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal
LA English

L3 ANSWER 56 OF 59 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1996:189901 CAPLUS
DN 124:278442
TI Suppression of proinflammatory cytokines in monocytes by a tetravalent guanylhydrazone
AU Bianchi, Marina; Bloom, Ona; Raabe, Tobias; Cohen, Pamela S.; Chesney, Jason; Sherry, Barbara; Schmidtmayerova, Helena; Calandra, Thierry; Zhang, Xini; et al.
CS Lab. Biomed. Sci., North Shore Univ. Hosp., Manhasset, NY, 11030, USA
SO Journal of Experimental Medicine (1996), 183(3), 927-36
CODEN: JEMEAV; ISSN: 0022-1007

PB Rockefeller University Press
DT Journal
LA English

L3 ANSWER 57 OF 59 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1996:77001 CAPLUS
DN 124:193144
TI High-performance liquid chromatographic method for guanylhydrazone compounds
AU Cerami, Carla; Zhang, Xini; Ulrich, Peter; Bianchi, Marina; Tracey, Kevin J.; Berger, Bradley J.
CS The Picower Institute for Medical Research, 350 Community Dr., Manhasset, NY, 11030, USA
SO Journal of Chromatography, B: Biomedical Applications (1996), 675(1), 71-5
CODEN: JCBBEP; ISSN: 0378-4347
PB Elsevier
DT Journal
LA English

L3 ANSWER 58 OF 59 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1995:896314 CAPLUS
DN 123:276077
TI Guanylhydrazones for treating cachexia and inflammatory and other conditions
IN Bianchi, Marina; Cerami, Anthony; Tracey, Kevin J.; Ulrich, Peter
PA Picower Institute for Medical Research, USA
SO PCT Int. Appl., 87 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9519767	A1	19950727	WO 1995-US828	19950119
	W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KE, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SI, SK, TJ, TT, UA, UZ, VN				
	RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 5599984	A	19970204	US 1994-315170	19940929
	AU 9518330	A1	19950808	AU 1995-18330	19950119
	AU 683999	B2	19971127		
	EP 746312	A1	19961211	EP 1995-910110	19950119
	EP 746312	B1	20020925		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 09508123	T2	19970819	JP 1995-519690	19950119
	AT 224707	E	20021015	AT 1995-910110	19950119
PRAI	US 1994-184540	A	19940121		
	US 1994-315170	A	19940929		
	WO 1995-US828	W	19950119		

OS MARPAT 123:276077

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---Logging off of STN---

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Executing the logoff script...

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	17.76	18.56

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-0.73	-0.73

STN INTERNATIONAL LOGOFF AT 17:02:37 ON 30 NOV 2005